

Amendments to the Specification

Please replace the paragraph beginning at page 9, line 9, with the following amended paragraph.

Figures ~~13A-B~~ 13A-C show two alternative formats for oligonucleotide probe capture. In Figure ~~13A~~ 13B, the addressable array-specific portions are on the allele-specific probe. Alleles are distinguished by capture of fluorescent signals on addresses Z1 and Z2, respectively. In Figure ~~13B~~ 13C, the addressable array-specific portions are on the common probe and alleles are distinguished by capture of fluorescent signals F1 and F2, which correspond to the two alleles, respectively.

Please replace the section beginning at page 24, line 7, through page 25, line 16, with the following amended section:

The 1,000 different addresses can be unique capture oligonucleotide sequences (e.g., 24-mer) linked covalently to the target-specific sequence (e.g., approximately 20- to 25-mer) of a LDR oligonucleotide probe. A capture oligonucleotide probe sequence does not have any homology to either the target sequence or to other sequences on genomes which may be present in the sample. This oligonucleotide probe is then captured by its addressable array-specific portion, a sequence complementary to the capture oligonucleotide on the addressable solid support array. The concept is shown in two possible formats, for example, for detection of the p53 R248 mutation (Figures ~~13A-B~~ 13A-C).

In Figures ~~13A-B~~ 13A-C, the top portion of the diagram shows two alternative formats for oligonucleotide probe design to identify the presence of a germ line mutation in codon 248 of the p53 tumor suppressor gene. The wild type sequence codes for arginine (R248), while the cancer mutation codes for tryptophan (R248W). The bottom part of the diagram is a schematic diagram of the capture oligonucleotide. The thick horizontal line depicts the membrane or solid surface containing the addressable array. The thin curved lines indicate a flexible linker arm. The thicker lines indicate a capture oligonucleotide sequence, attached to the solid surface in the C to N direction. For illustrative purposes, the capture oligonucleotides are drawn vertically, making the linker arm in section B appear "stretched". Since the arm is flexible, the capture oligonucleotide will be able to hybridize 5' to C and 3' to N in each case, as dictated by base pair complementarity. A similar orientation of oligonucleotide hybridization would be allowed if the oligonucleotides were attached to the membrane at the N-terminus. In this case, DNA/PNA hybridization would be in standard

antiparallel 5' to 3' and 3' to 5'. Other modified sugar-phosphate backbones would be used in a similar fashion. Figures 13A-B ~~13A~~ shows two LDR primers that are designed to discriminate wild type and mutant p53 by containing the discriminating base C or T at the 3' end. In the presence of the correct target DNA and *Tth* ligase, the discriminating probe is covalently attached to a common downstream oligonucleotide. The downstream oligonucleotide is fluorescently labeled. The discriminating oligonucleotides are distinguished by the presence of unique addressable array-specific portions, Z1 and Z2, at each of their 5' ends. A black dot indicates that target dependent ligation has taken place. After ligation, oligonucleotide probes may be captured by their complementary addressable array-specific portions at unique addresses on the array. Both ligated and unreacted oligonucleotide probes are captured by the oligonucleotide array. Unreacted fluorescently labeled common primers and target DNA are then washed away at a high temperature (approximately 65°C to 80°C) and low salt. Mutant signal is distinguished by detection of fluorescent signal at the capture oligonucleotide complementary to addressable array-specific portion Z1, while wild type signal appears at the capture oligonucleotide complementary to addressable array-specific portion Z2. Heterozygosity is indicated by equal signals at the capture oligonucleotides complementary to addressable array-specific portions Z1 and Z2. The signals may be quantified using a fluorescent imager. This format uses a unique address for each allele and may be preferred for achieving very accurate detection of low levels of signal (30 to 100 attomoles of LDR product). Figure ~~13B~~ 13C shows the discriminating signals may be quantified using a fluorescent imager. This format uses a unique address where oligonucleotide probes are distinguished by having different fluorescent groups, F1 and F2, on their 5' end. Either oligonucleotide probe may be ligated to a common downstream oligonucleotide probe containing an addressable array-specific portion Z1 on its 3' end. In this format, both wild type and mutant LDR products are captured at the same address on the array, and are distinguished by their different fluorescence. This format allows for a more efficient use of the array and may be preferred when trying to detect hundreds of potential germline mutations.